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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/685,053	10/06/2000	David M. Armistead	A-748E	3146

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U.S. PATENT OPERATIONS/JWB
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EXAMINER
BALASUBRAMANIAN, VENKATARAMAN

ART UNIT	PAPER NUMBER
1624	9

DATE MAILED: 11/05/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/685,053	ARMISTEAD ET AL.	
	Examiner	Art Unit	
	Venkataraman Balasubramanian	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the c rrespondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 August 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-9,22-26,28 and 29* is/are rejected.

7)☒ Claim(s) *2-4,10-21 and 27* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicants' response, which included cancellation of claims 30-31 and amendment to claims 1-29, filed on 3/20/2002, is made of record.

Claims 1-29 are now pending.

In view of applicants' amendment, all 112 rejections made in the previous office action have been obviated.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 24-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating angiogenesis, does not reasonably provide enablement for treating all diseases embraced in the claim language of the instant invention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant claims are drawn to 'a method for treating kinase–mediated disease or disease symtopms. Method claims 24-26 are not adequately enabled for the range of diseases recited therein. From the reading of specification, it appears that the applicants are asserting that the embraced compounds because of their mode action, which involves inhibition of kinase(s), would be useful for all sorts of diseases including autoimmune diseases, cancer, Alzheimer's disease, various arthritis, multiple sclerosis

etc. However, the applicants have not provided any competent evidence that the instantly disclosed tests are highly predictive for all the uses disclosed and embraced by the claim language for the intended mammal. That a single class of compounds can be used to treat all diseases embraced in the claims is an incredible finding for which applicants have not provided supporting evidence. Moreover many if not most of diseases such as rheumatoid arthritis, multiple sclerosis, Alzheimer's disease etc. are very difficult to treat and hardly possible to prevent as claimed herein. For multiple sclerosis alone there is no known drug, which can successfully reverse the course of the disease, despite the fact that there are many drugs, which can be used for "inflammatory condition". Note substantiation of utility and its scope is required when utility is "speculative", "sufficiently unusual" or not provided. See Ex parte Jovanovics, 211 USPQ 907, 909; In re Langer 183 USPQ 288 . Also note Hoffman v. Klaus 9 USPQ 2d 1657 and Ex parte Powers 220 USPQ 925 regarding type of testing needed to support in vivo uses. Next, applicant's attention is drawn to the Revised Interim Utility and Written Description Guidelines, at 64 FR 71427 and 71440 (December 21, 1999) wherein it is emphasized that 'a claimed invention must have a specific and substantial utility'. The disclosure in the instant case is not sufficient to enable the instantly claimed 'preventive' effect solely based on the inhibitory activity disclosed for the compounds. The state of the art is indicative of the requirement for undue experimentation. See Traxler (provided).

In evaluating the enablement question, several factors are to be considered. Note In re Wands, 8 USPQ2d 1400 and Ex parte Forman, 230 USPQ 546. The factors

include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1) The nature of the invention: Therapeutic use of the compounds in treating all diseases due to kinase inhibitory activity.

2) The state of the prior art: Although there are several kinase inhibitors known, they have not been able to treat all diseases embraced in the instant claims.

3) The predictability or lack thereof in the art: Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use for the 'treatment of all kinase mediated diseases' of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

4) The amount of direction or guidance present and 5) the presence or absence of working examples: There is no supporting evidence that all diseases embraced are treatable in view of their kinase activity.

6) The breadth of the claims: The instant claims embrace treatment of all or any diseases by inhibiting all or any kinase

7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan, regarding the pharmaceutical use, for the reasons stated above. Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims. In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of ligand-receptor interactions in general, and the lack of working examples regarding the activity of the claimed compounds towards 'preventing' the variety of diseases of the instant claims, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 6, 8, 22 and 28-29 are rejected under 35 U.S.C. 102(b) as being anticipated by Giraldi et al. US 3,074,943 for reasons of record. To repeat:

Giraldi et al. teaches several substituted triazines for use as anti viral agents, which include compounds generically claimed in the instant claims. See formula I and note the definition of R', R", and R"' on col.1. Note when R"' is hydrogen, the

compounds taught by Giraldi include those claimed in the instant claims. See examples 1-5 for compounds made and the intermediates used for making on col.2-3.

Claims 1, 5-8, 22 and 28-29 are rejected under 35 U.S.C. 102(b) as being anticipated by Cutler et al. US 3,097,205 for reasons of record. To repeat:

Cutler et al. teaches several disubtituted triazines, which include those, claimed in the instant claims for use as antibacterial agents. See formula I, III, IV, V, VI, VII and VII and note the definition of Y, Z and Z' on col. 1 through col. 3. Note the definition of Y, Z and Z' corresponds to instant R^1 and R^2. Also note the various choices of Z and Z' on col.2 and the process of making. See col. 3 –col.9 for examples of compounds made.

Claims 1, 6, 23 and 28-29 are rejected under 35 U.S.C. 102(b) as being anticipated by Cutler et al. US 3,209,003

Cutler et al. teaches several disubtituted triazines, which include those, claimed in the instant claims for use as antibacterial, antifungal and antiviral agents. See formula I and note the definition of X, R, Y^1 and Y^2 on col.1. Note the definition of X, R, Y^1 and Y^2 corresponds to compounds of instant R^1 and R^2. See examples 1-25 for various compounds made shown on col. 5 through 11.

All the above three rejections were same as made in the previous office action.

Applicants' argument to overcome this rejection by provisos in claim 1 and 17 is not persuasive, as these provisos do not obviate the 102 rejections. Not the provisos limits R^1 but R^1 and R^2 are independently can be the same group. Thus instant R^2 can be the amino and R^1 the other group embraced in the above said references. Hence the

instant claims are anticipated by the references and the rejections are therefore maintained.

Claims 1, 6, 23, and 28-29 are rejected under 35 U.S.C. 102(b) as being anticipated by Cutler et al. US 3,209,003 for reasons of record. To repeat:

Cutler et al. teaches several disubtituted triazines, which include those, claimed in the instant claims for use as antibacterial, antifungal and antiviral agents. See formula I and note the definition of X, R, Y^1 and Y^2 on col.1. Note the definition of X, R, Y^1 and Y^2 corresponds to compounds of instant R^1 and R^2. See examples 1-25 for various compounds made shown on col. 5 through 11.

Contrary to applicants' urging there appears to be no provisos in claims 1 and 17 to exclude the compound taught by the above art. Note also the reference teaches substituted phenyl compounds. In view of this, the rejection is maintained.

Applicants should also note that in amending the claims to overcome the 102 rejection should also address possible obviousness type 103 rejection as each of these references teaches a genus and equivalency of the exemplified compounds with those claimed in the genus.

Claims 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Fischer US 3,855,220.

This rejection is obviated in view of applicants' amendment to claim 1.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 6, and 8-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Newton et al. US 5,062,882 for reasons of record. To repeat:

Newton et al. teaches several substituted triazines for use as herbicides. See formula I on col. 1 and note the definition of X, Y, Z, R1 and R^2. Note when one of R^1 and R^2 group is hydrogen, the compounds taught by Newton et al. include those claimed in the instant claims. See examples 1-72 on col.5-18 for compounds made.

Instant claims recite disubstituted triazine, i.e. the third substituent on the triazine carbon is hydrogen. Newton et al. does not teach hydrogen for either of R^1 and R^2 in compounds made.

However Newton et al. teaches the equivalency of exemplified substituents for R^1 and R^2 groups with that claimed. See cols.1, formula I, especially the definitions of R^1 and R^2 groups. As one trained in the art would expect the species of the genus behave similarly and possess the same use, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to make compounds variously substituted in triazine ring including species bearing hydrogen for R^1 or R^2 group as permitted by the reference and expect resulting compounds to possess the uses taught by the art in view of the equivalency teaching outline above.

Applicants' argument to overcome this rejection is not persuasive. The cited art teaches use of the compounds, as herbicides and one would be motivated to make the compounds embraced by the genus for the same herbicidal activity. The fact that

another use for the compounds embraced is found later does negate the motivation to make and use the compounds for the said utility. Furthermore, the compounds taught by the reference cannot be deemed as novel if additional uses were found for the same compound. As for applicants argument that one would be motivated to move away form the teaching ahs no valid basis merely showing that some compounds are less active than other. Not there are 72 compounds tested and applicants sampling 8-11 is a biased sampling.

Hence the rejection is proper and is maintained.

Claims 1 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Riebel et al. US 6,284,710 (equivalent DE 196 41 693) for reasons of record. To repeat:

Riebel et al. teaches several substituted triazines for use as herbicides. See formula I on col. 1 and note the definition of X, Y, Z, R^1 and R^2. Note when Z is hydrogen, compounds taught by Riebel et al. include those claimed in the instant claims. See col. 6 through col. 58 for compounds made.

Instant claims recite disubstituted triazine, i.e. the third substituent on the triazine carbon is hydrogen. Riebel et al. does not teach hydrogen for Z in compounds made.

However Riebel et al. teaches the equivalency of exemplified substituents for Z groups with that claimed. See cols.1, formula I, especially the definition Z groups. As one trained in the art would expect the species of the genus behave similarly and possess the same use, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to make compounds variously substituted in triazine ring including species bearing hydrogen for Z group as permitted by the

reference and expect resulting compounds to possess the uses taught by the art in view of the equivalency teaching outline above.

Applicants' argument to overcome this rejection is not persuasive. Contrary to applicants' urging there several compounds in the Table, which are no toxic to beneficial crops such as corn wheat barley etc, and that some variation in activity would lead one trained in the art consider the entire genus taught by Riebel et al. to be devoid of the use taught.

Hence the rejection is proper and is maintained.

Allowable Subject Matter

Claims 2-4, 10-21, and 27 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Said claims would be allowed since specific species and the method of use of these species embraced in these claims are not taught or suggested by the art of record or from a search in the relevant art area.

This action is not made FINAL.

Conclusion

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (703) 305-1674. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is Mukund Shah whose telephone number is (703) 308-4716.

The fax phone number for the organization where this application or proceeding is assigned (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

V. Balasubramanian
Venkataraman Balasubramanian

10/29/2002